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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	PAPER NUMBER
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/784,870	TAKAIWA ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-17,19-31,33 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-17, 19-31, 33-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 7-17, 19-31, 33-34 are currently pending in this application.

Applicants' amendments and arguments filed on 9-8-06, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-17, 19-31, 33-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding a polypeptide with SEQ ID NO:1 or 2 and having a specific protease activity, vectors and host cells comprising said polynucleotide and a method of making the polypeptide using the host cell comprising said polynucleotide, does not reasonably provide enablement for any such polynucleotide which encodes a polypeptide that is at least 90% identical to SEQ ID NO:1 or 2 and encoding a polypeptide having protease activity, vectors and host cells comprising said polynucleotide and a method of making the polypeptide using the host cell comprising said polynucleotide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1)

the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 7-17, 19-31, 33-34 are so broad as to encompass any polynucleotide that encodes a polypeptide that is at least 90% identical in its sequence to SEQ ID NO:1 or 2 vectors and host cells comprising said polynucleotide and a method of making the polypeptide using the host cell comprising said polynucleotide. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by said polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in said encoded protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. Simply put, applicants have not taught those skilled in the art as to where exactly on the polynucleotide sequence encoding SEQ ID NO:1 or 2, specific nucleotides can be modified (i.e., by insertion, deletion or substitution), and how to select those modified sequences in order to arrive at those that encode the polypeptide having the specific activity of SEQ ID NO:1 or 2. The specification is limited to teaching the use of the polynucleotide with SEQ ID NO:3 or 4 to encode the polypeptide with SEQ ID NO:1 or 2 and use it as a specific protease but provides no guidance with regard to the making of variants and mutants or with regard to the

other uses indicated above. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a polynucleotide sequence leading to variants or mutants through which amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any encoded protein, and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide encoding a polypeptide with 90% sequence identity to SEQ ID NOS:1 or 2 because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without affecting its activity of encoding the polypeptide having the specific protease activity; (B) the general tolerance of polynucleotides encoding such proteases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide on the polynucleotide encoding said protease

with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful .

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides with an enormous number of nucleotide modifications to the polynucleotides encoding SEQ ID NOS: 1 or 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the above rejection, applicants traverse. Applicants submit that determining what sequences fall within or without the scope of present claims would be readily apparent to the skilled artisan without undue experimentation when these claims are read in view of the specification, as well as the knowledge generally available in the art. Applicants argue that the specification at pages 5-7, provides a description of the scope of homology permissible in the claimed alkaline protease. Applicants also maintain that the Table appearing on page 6 of the specification, provides guidance for the artisan by providing a detailed listing of preferable amino acids for each Xaa within the claimed amino acid sequences (in particular SEQ ID NO:2). Examiner respectfully disagrees. This is not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis,

etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., a polynucleotide encoding a polypeptide that is 90% identical to SEQ ID NO:1) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. While Examiner agrees that Table on page 6 provides suggestion for amino acids that can be substituted in specific positions, it falls short of encompassing all the changes that one has to make for arriving at polynucleotides encoding sequences that are 90% identical to SEQ ID NO:1. Examiner would have no objection if applicants limit their claims to the specific mutants recited in page 6. Applicants also base their arguments on a previously allowed parent application drawn to a polypeptide sequence. Examiner has no comments on issued applications and reminds the applicant that each application is examined independently applying the rules and guidance available at the time of examination. An allowed application does not bind the Examiner's action in a application that is being considered at this time.

As previously stated the specification does not establish: (A) regions of the polynucleotide structure which may be modified without affecting its activity of encoding the polypeptide having the specific protease activity; (B) the general tolerance of polynucleotides encoding such proteases to modification and extent of such tolerance; (C) a rational and predictable scheme for

modifying any nucleotide on the polynucleotide encoding said protease with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful . Therefore the above rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7-17, 19-31, 33-34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-20 of U.S. Patent No. 6,376,227 and claims drawn to "a gene" in copending applications 10/456479, 10/820712, 10/820714, 11/235249,11/318576. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim, because the examined claim is either anticipated by, or would have been obvious over the reference claim. See, e.g., *In re Berg*, 140 F.3d 1428,46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi* 759 F.2d 887,225 USPQ 645 (Fed. Cir. 1985). Although the conflicting

claims are not identical, they are not patentably distinct from each other. Claims 7-17, 19-31, 33-34 of the instant application and claims 4-20 of the reference patent and claims drawn to "a gene" of the copending applications are all directed to polynucleotides encoding polypeptides that have at least 90% sequence identity with SEQ ID NO:1 or 2 (see enclosed sequence alignments). Among all the different polynucleotides claimed in the instant application and in the reference patent and copending applications a number of polynucleotides are identical to one another. The portion of the specification (and the claims) in the reference patent and copending applications that supports the recited polynucleotides includes several embodiments that would anticipate the polynucleotides and the vectors an host cells claimed in claims 7-17, 19-31, 33-34 herein. Claims 7-17, 19-31, 33-34 of the instant application listed above cannot be considered patentably distinct over claims 4-20 of the reference patent and claims of the copending applications when there is specifically recited embodiment that would anticipate mainly claims 7-17, 19-31, 33-34 of the instant application. Alternatively, claims 7-17, 19-31, 33-34 cannot be considered patentably distinct over claims 4-20 of the reference patent and claims of the co-pending applications when there is specifically disclosed embodiment in the reference patent and reference applications that supports claims 4-20 of that patent (and said applications) and falls within the scope of claims 7-17, 19-31, 33-34 herein because it would have been obvious to one having ordinary skill in the art to modify claims 4-20 of the reference patent and the claims drawn to a "gene" in the cop[ending applications by selecting a specifically disclosed embodiment that supports those claims. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within claims of the reference patent and applications.

Conclusion

None of the claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

January 29, 2007